

Cancer Vaccines  
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## ABSTRACTS

Ovarian Cancer Research Notebook.

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2003

Vaccine for Cervical Cancer on the Horizon.

ABC News.

2002;August 1, 2002

Cancer vaccine competition wide open as agents move rapidly into clinical arena.

Anon.

J Natl Cancer Inst. 1999;1999 Feb 17 17

Health: Cervical Cancer Vaccine on the Way.

BBC News.

BBC News. 1999

Biomira. News Release: Theratope Vaccine Featured on ABC Lifetime Cable Television Special 1999.

Biomira.

Biomira News Release: Theratope Vaccine Featured on ABC Lifetime Cable Television Special 1999 ([Http://Www Biomira Com/News/DetailNewsRelease/67/](http://www.biomira.com/news/detailnewsrelease/67/)). 1999

Colon Cancer Vaccine Ready to Test 2000.

Bonfield T.

2000

Vaccines for Ovarian Carcinoma.

Butts CS.

*Cancer Control*. 1999 Jul; 6(4):335-42.

**BACKGROUND:** Metastasis to the abdominal cavity is the primary cause of morbidity and mortality in patients with ovarian cancer. Beyond surgery and chemotherapy combinations, strategies that target tumor cells in vivo are being investigated, such as the use of recombinant cytokines to up-regulate or modulate the cell-mediated or humoral immune response. **METHODS:** The authors report on their experience with tumor vaccines, including first-generation vaccines, peptide vaccines, and polynucleotide vaccines, in the treatment of ovarian cancer. **RESULTS:** Cytokines may stimulate proliferation or activation of effector cells that mediate either major histocompatibility restricted cytotoxicity (adaptive immunity) or natural (innate) immunity.

Cytokines are often pleiotropic, and their effects may depend on concentration, scheduling, and responsiveness of the cell populations to which they are directed. They also have been used to enhance the efficacy of tumor vaccines that have reached a higher level of sophistication. Recently designed tumor vaccines are capable of stimulating antitumor immune responses that recognize tumor cell epitopes or that have the potential to act synergistically with cytokines such as interleukin-2 and interleukin-12. CONCLUSIONS: Enthusiasm for antitumor vaccine strategies is supported by accumulating clinical reports of responses following treatments using a variety of vaccines. Additional research is needed to determine optimum vaccine approaches for the treatment or prevention of ovarian cancer

The beginning of the end for cervical cancer?

Crum CP.

*N Engl J Med.* 2002 Nov 21; 347(21):1703-5.

Dendritic Cell Immunotherapy May Provide Cancer Patients with a Vaccine to Combat Malignant Brain Tumors 1999.

CSMC.

(<http://www.sciencedaily.com/releases/1999/01/990125073302.htm>). 1999

The use of vaccines in the prevention and treatment of cervical cancer.

Davidson EJ, Kitchener HC, Stern PL.

*Clin Oncol (R Coll Radiol).* 2002 Jun; 14(3):193-200.

The close association between high risk HPV infection and cervical carcinoma has provided the impetus for the development of prophylactic and therapeutic vaccination schedules. An effective prophylactic vaccine would obviate the need for population-based cervical screening programmes, while therapeutic vaccination might provide an effective adjunct to or replacement for conventional treatment for benign and malignant cervical disease. While the challenges associated with the design and implementation of immunotherapies are numerous, optimism remains high and it is expected that the next few decades will witness a revolutionary change in the way we treat cervical cancer and its premalignant lesions. A papillomavirus vaccine that prevented HPV infection on the one hand and acted against established disease on the other, would have a profound impact on one of the major cancers affecting women globally

[Negative results of a randomized therapeutic trial of nonspecific immunotherapy in primary, surgically-treated non-small cell bronchial cancer].

Decroix G, Chastang C, Lebeau B, et al.

*Rev Mal Respir.* 1984; 1(1):25-30.

Between March 1978 and May 1981, 219 patients suffering from non-small cell primary bronchial carcinoma underwent surgical excision which was intended to be curative. Three weeks later the patients were randomised into two groups: 1. A control group, with no other treatment following excision (110 patients). 2. A non-specific immunotherapy group (109 patients). The immunostimulant used was an aqueous suspension of heat killed mycobacterium smegmatis administered subcutaneously once a month. The trial was analysed on December 1, 1982. There were 117 recurrences and 112 deceased. There was no significant difference as regard survival without relapse or overall survival; all causes of death were included

[Human papillomavirus: a vaccine against cervical carcinoma uterine].

Franceschi S.

*Epidemiol Prev.* 2002 May; 26(3):140-4.

Human papillomavirus (HPV) has been identified in fewer than 20 years as the central cause of cervical carcinoma and one of the most powerful known human carcinogens. At least 20 different types of HPV have been associated with relative risks of approximately 100 for both squamous-cell carcinoma and the rarer adenocarcinoma of the cervix uteri. Cytologic screening programs have contributed to the decline of cervical cancer mortality in Europe and the United States. Long-term screening programs remain, however, outside the reach of the poorest countries, where 80% of deaths for cervical carcinoma occurs. More than 20 different types of prophylactic and/or therapeutic vaccines against HPV are being evaluated in clinical or preclinical

studies. One such type, a prophylactic vaccine based on the marked immunogenicity and safety of the empty viral capsid, will start being evaluated in 2002 in 3 phase-III randomized studies, mostly in the United States and Latin America. The International Agency for Research on Cancer and World Health Organization are planning, in parallel with the studies above, a double blind randomized phase IV study of approximately 40,000 adolescent and young women in Asia. Such study, which should include a cluster randomization (by village of birth); a comparison with another vaccine (rather than with placebo); and, possibly, the inclusion of adolescents and young adults of male sex. Such trial may accelerate by many years the availability of an anti-HPV vaccine among populations at highest risk for cervical carcinoma

Human papilloma virus (HPV) and cervical cancer.

Furumoto H, Irahara M.

*J Med Invest.* 2002 Aug; 49(3-4):124-33.

Epidemiological and experimental studies have clearly shown that high-risk HPV infection is the main etiologic factor for cervical cancer. Recent studies have indicated that the E6 and E7 gene products play a critical role in cervical carcinogenesis. The E6 and E7 products interfere with the p53 and pRB functions, respectively, and deregulate the cell cycle. The HPV DNA is integrated into the host's chromosomes with disruption of the E2 gene. This disruption promotes the expression of E6 and E7, leading to the accumulation of DNA damage and the development of cervical cancer. The study of the immune response against HPV has been hampered by the lack of a cell culture system for the virus. A breakthrough was made by the discovery that a major capsid protein L1 self-assembles into virus-like particles (VLP) when expressed in eukaryotic systems. Clinical trials of VLP-based vaccines are in progress, and DNA vaccines for the HPV surface protein genes are under development. The E7 and E6 oncoproteins are attractive targets for cancer immunotherapy because their expression is required to maintain the oncogenicity of cervical cancer cells. Cancer immunotherapy for cervical cancer with vaccinations of E7 peptides or dendritic cell-based immunotherapy is moving toward clinical trials

Dendritic Cell Vaccine Helps Fight Children's Cancer 2001.

Geiger JD.

2001

Adjuvant active specific immunotherapy of stage II and stage III colon cancer with an autologous tumor cell vaccine: first randomized phase III trials show promise.

Hanna MG, Jr., Hoover HC, Jr., Vermorken JB, et al.

*Vaccine.* 2001 Mar 21; 19(17-19):2576-82.

We performed three multi-institutional, prospectively randomized, controlled clinical trials, assessing the therapeutic effect of post-resection adjuvant active specific immunotherapy in patients with stage II and stage III colon cancer. In each study four outcomes were considered: time-to-disease recurrence, overall survival intervals, disease-free survival intervals, and recurrence-free survival intervals using the Kaplan-Meier method for generating curves and the log-rank test used to compare efficacy distributions. In addition, a meta-analysis of the three phase III trials was performed since the trials had proven homogeneity. Two main analyses were performed: (1) the intent-to-treat colon cancer patients from all three studies; and (2) analyzable colon cancer patients in all three studies. The conclusion of these analyses is that adjuvant active specific immunotherapy provided significant clinical benefits in patients with stage II colon cancer and appears to be an important new adjuvant treatment for these patients

Theratope vaccine (STn-KLH).

Holmberg LA, Sandmaier BM.

*Expert Opin Biol Ther.* 2001 Sep; 1(5):881-91.

Active specific immunotherapy (ASI) is a promising approach to treating cancer. Numerous studies in the laboratory have demonstrated that various cancer vaccines can stimulate antibody and cell mediated immune responses against tumour-associated antigens [1-9]. Yet few studies have demonstrated convincing clinical responses. Sialyl-Tn (STn) is a carbohydrate associated with the MUC1 mucin on a number of human cancer cells and is associated with more aggressive disease. Consequently, STn is an ideal candidate for ASI therapy. Theratope vaccine is a cancer vaccine that was designed by Biomira, Inc. (Edmonton, Alberta, Canada) by incorporating a synthetic STn antigen that emulates the carbohydrate seen on human

tumours. The clinical trials conducted to date with Theratope vaccine are outlined in this report. Overall, Theratope vaccine has been well-tolerated with minimal toxicity. The most common side effects have been in duration and erythema at the site of injections. Both in a non-transplant setting following low dose iv. cyclophosphamide and high dose autologous transplant setting, there has been a trend toward Theratope vaccine decreasing the risk for relapse, prolonging the time to relapse and thus impacting on overall survival. The definitive Phase III trial comparing the outcome of patients with metastatic breast cancer receiving vaccinations with Theratope vaccine versus vaccination with the nonspecific immune stimulants Keyhole Limpet Hemocyanin (KLH) and Detox -B stable emulsion (Detox-B) (now called Enhanzyn Immunostimulant) was closed to enrolment on March 30, 2001. Over 1000 women with distant metastatic breast cancer were enrolled into the program

Tumor-specific idiotypic vaccines in the treatment of patients with B-cell lymphoma--long-term results of a clinical trial.

Hsu FJ, Caspar CB, Czerwinski D, et al.

*Blood.* 1997 May 1; 89(9):3129-35.

The surface Ig on each B-cell lymphoma has unique portions (idiotypes), which can be recognized by the immune system. In this study, we immunized patients against the Ig expressed by their tumor and observed their clinical outcomes. After standard chemotherapy, 41 patients with non-Hodgkin's B-cell lymphoma received a series of injections with a vaccine consisting of tumor Ig protein coupled to keyhole limpet hemocyanin and emulsified in an immunologic adjuvant. Subjects were observed for toxicity, immune responses, and tumor status. The median duration of follow-up of all patients is 7.3 years from diagnosis and 5.3 years from the last chemotherapy given before vaccine treatment. Twenty patients (49%) generated specific immune responses against the idiotypes of their tumor Ig. Two patients who had residual disease experienced complete tumor regression in association with the development of these immune responses. The median duration of freedom from disease progression and overall survival of all 20 patients mounting an anti-idiotypic immune response are significantly prolonged compared to the patients who did not mount an immune response. Thirty-two patients were in their first remission and nine were in subsequent remissions before beginning vaccine treatments. Analysis of the 32 first remission patients also shows an improved clinical outcome for those patients who mounted a specific immune response compared to those who did not (freedom from progression, 7.9 years v 1.3 years  $P = .0001$ ; median survival from time of last chemotherapy not yet reached v 7 years,  $P = .04$ ). This study confirms an earlier report that patients with B-cell lymphoma can be induced to make a specific immune response against the Ig expressed by their own tumor. It further shows that the ability to make such an immune response is correlated with a more favorable clinical outcome. Prospective controlled trials will be needed to prove a causal relationship between anti-idiotypic immunity and improved clinical outcome

A controlled trial of a human papillomavirus type 16 vaccine.

Koutsky LA, Ault KA, Wheeler CM, et al.

*N Engl J Med.* 2002 Nov 21; 347(21):1645-51.

**BACKGROUND:** Approximately 20 percent of adults become infected with human papillomavirus type 16 (HPV-16). Although most infections are benign, some progress to anogenital cancer. A vaccine that reduces the incidence of HPV-16 infection may provide important public health benefits. **METHODS:** In this double-blind study, we randomly assigned 2392 young women (defined as females 16 to 23 years of age) to receive three doses of placebo or HPV-16 virus-like-particle vaccine (40 microg per dose), given at day 0, month 2, and month 6. Genital samples to test for HPV-16 DNA were obtained at enrollment, one month after the third vaccination, and every six months thereafter. Women were referred for colposcopy according to a protocol. Biopsy tissue was evaluated for cervical intraepithelial neoplasia and analyzed for HPV-16 DNA with use of the polymerase chain reaction. The primary end point was persistent HPV-16 infection, defined as the detection of HPV-16 DNA in samples obtained at two or more visits. The primary analysis was limited to women who were negative for HPV-16 DNA and HPV-16 antibodies at enrollment and HPV-16 DNA at month 7. **RESULTS:** The women were followed for a median of 17.4 months after completing the vaccination regimen. The incidence of persistent HPV-16 infection was 3.8 per 100 woman-years at risk in the placebo group and 0 per 100 woman-years at risk in the vaccine group (100 percent efficacy; 95 percent confidence interval, 90 to 100;  $P < 0.001$ ). All nine cases of HPV-16-related cervical intraepithelial neoplasia occurred among the placebo recipients. **CONCLUSIONS:** Administration of this HPV-16 vaccine reduced the incidence of both HPV-16 infection and HPV-16-related cervical intraepithelial neoplasia. Immunizing HPV-16-negative women may eventually reduce the incidence of cervical cancer

Mercola.com 2002. Cervical Cancer Vaccine -- A Shameful Example of How Medical Research is Taking Dangerous Short-Cuts.

Mercola J.

2002

Nonspecific immunotherapy of malignant tumors.

Milas L, Withers HR.

*Radiology*. 1976 Jan; 118(1):211-8.

At present, nonspecific immunotherapy of malignant tumors seems to be the most promising among immunotherapeutic modalities. Potent nonspecific immunostimulants, Bacillus Calmette-Guerin (BCG) and *Corynebacterium parvum*, exhibit an antitumor activity in experimental animals, which is commonly manifested by reduced tumor growth and sometimes by complete regression of tumors. Antitumor effectiveness of these bacteria is largely related to tumor immunogenicity and host immunocompetence. Recently, BCG has frequently been used for clinical immunotherapy and has provided therapeutic benefit in many instances, particularly when combined with chemotherapy, radiotherapy or surgery. Clinical experience with *C. parvum* is so far limited

Breakthrough Medical Diagnostics Technology: The Polymerase Chain Reaction (PCR).

Mordechai E.

1999

A phase I trial of a human papillomavirus (HPV) peptide vaccine for women with high-grade cervical and vulvar intraepithelial neoplasia who are HPV 16 positive.

Muderspach L, Wilczynski S, Roman L, et al.

*Clin Cancer Res*. 2000 Sep; 6(9):3406-16.

Eighteen women with high-grade cervical or vulvar intraepithelial neoplasia who were positive for human papillomavirus (HPV) 16 and were HLA-A2 positive were treated with escalating doses of a vaccine consisting of a 9-amino acid peptide from amino acids 12-20 encoded by the E7 gene emulsified with incomplete Freund's adjuvant. Starting with the eleventh patient, an 8-amino acid peptide 86-93 linked to a helper T-cell epitope peptide with a covalently linked lipid tail was added. Patients with colposcopically and biopsy-proven cervical intraepithelial neoplasia/vulvar intraepithelial neoplasia II/III received four immunizations of increasing doses of the vaccine each 3 weeks apart, followed by a repeat colposcopy and definitive removal of dysplastic tissue 3 weeks after the fourth immunization. Patients were skin tested with the E7 12-20 peptide as well as control candida, mumps, and saline prior to and after the series of immunizations. Peripheral blood mononuclear cells were obtained by leucopheresis prior to and after the series of immunizations for analyses of CTL reactivity to the E7 12-20 and 86-93 epitope sequences. The presence of HPV 16 was assessed by DNA PCR on cervical scrapings and the biopsy specimens after vaccination. Pathology specimens were analyzed before and after vaccination for the presence of dysplasia, and the intralesional infiltrate of CD4/CD8 T-cells and dendritic cells was measured by immunohistochemical staining. Only 3 of 18 patients cleared their dysplasia after vaccine, but an increased S100+ dendritic cell infiltrate was observed in 6 of 6 patients tested. Cytokine release and cytolysis assays to measure E7-specific reactivity revealed increases in 10 of 16 patients tested. No positive delayed type hypersensitivity skin test reactivity was shown in any patient to HPV E7 12-20 before or after vaccinations. Virological assays showed that 12 of 18 patients cleared the virus from cervical scrapings by the fourth vaccine injection, but all biopsy samples were still positive by in situ RNA hybridization after vaccination. Six patients had partial colposcopically measured regression of their cervical intraepithelial neoplastic lesions in addition to the three complete responders. The data establish that a HPV-16 peptide vaccine may have important biological and clinical effects and suggest that future refinements of an HPV vaccine strategy to boost antigen-specific immunity should be explored

Regression of tumors in mice vaccinated with professional antigen-presenting cells pulsed with tumor extracts.

Nair SK, Snyder D, Rouse BT, et al.

*Int J Cancer*. 1997 Mar 17; 70(6):706-15.

Vaccination with tumor extracts circumvents the need to identify specific tumor rejection antigens and extends the use of active immunotherapy to the vast majority of cancers, in which specific tumor antigens have not yet been identified. In this study we examined the efficacy of tumor vaccines comprised of unfractionated tumor material presented by professional antigen-presenting cells (APC): dendritic cells (DC) or macrophages (M phi). To enhance the relevance of these studies for human patients we used 2 poorly immunogenic murine tumor models and evaluated the effectiveness of the vaccination protocols in tumor-bearing animals. APC (in particular DC) pulsed with unfractionated extracts from these "poorly immunogenic" tumors were highly effective in eliciting tumor-specific cytotoxic T lymphocytes. A measurable CTL response could be detected after even a single immunization with tumor extract-pulsed DC. DC or M phi pulsed with tumor extract were also effective vaccines in tumor-

bearing animals. In the murine bladder tumor (MBT-2) model a modest extension of survival and 40% cure rate was seen in the animal groups immunized with DC or M phi pulsed with MBT-2 tumor extract. DC or M phi pulsed with B16/F10.9 tumor extract were also remarkably effective in the B16 melanoma lung metastasis model, as shown by the observation that treatment with APC caused a significant reduction in lung metastases. Cumulatively, the CTL and immunotherapy data from the two murine tumor systems suggest that APC (in particular DC) pulsed with unfractionated cell extracts as a source of tumor antigen may be equally or more effective than genetically modified tumor vaccines

Antitumor Vaccine.

RESAN.

2002

Vaccine Aimed at Cervical Cancer Shows Promise.

Reuters.

2002

Vaccines Show Promise Against Melanoma.

Rosenberg S.

1998; 1998 Mar 2

Peptide and carbohydrate vaccines in relapsed prostate cancer: immunogenicity of synthetic vaccines in man--clinical trials at Memorial Sloan-Kettering Cancer Center.

Slovin SF, Scher HI.

*Semin Oncol.* 1999 Aug; 26(4):448-54.

Men with rising prostate-specific antigen (PSA) levels after primary therapies such as prostatectomy or radiotherapy represent a unique group for whom no standard treatment option exists. A variety of approaches including expectant monitoring, dietary modification, hormonal therapy, and alternative medicines have shown an impact on the rate of increase in PSA, but the overall effect on survival remains controversial. At Memorial Sloan-Kettering Cancer Center, we have focused our treatment approach on this cohort of patients in a series of phase I monovalent carbohydrate and glycoprotein-conjugate vaccine trials using the patients' immune system to generate an antitumor response. These synthetic vaccines are conjugated to keyhole limpet hemocyanin (KLH) and given with the immunologic adjuvant QS21 as five subcutaneous vaccines over 26 weeks. All patients generated specific high-titer immunoglobulin M (IgM) and/or IgG antibodies, some of which were able to mediate complement lysis. Preliminary data suggest that these vaccines may impact on the rate of increase in posttreatment PSA slopes compared with pre-PSA values. The impact of vaccine therapy on the PSA slope and its effect on the time to radiographic progression are the current focus of a forthcoming phase II trial. Vaccines may offer an alternative treatment option for the patient who has relapsed early following primary therapies

Experimental Vaccine for Cervical Cancer to Be Tested at Saint Louis University.

SLU.

1998

Cervical cancer vaccines: progress and prospects.

Steller MA.

*J Soc Gynecol Investig.* 2002 Sep; 9(5):254-64.

Cervical cancer remains a leading cause of cancer-related mortality in women, particularly in developing countries. The causal association between genital human papillomavirus (HPV) infection and cervical cancer has been firmly established and the oncogenic potential of certain HPV types has been clearly demonstrated. In recognition of the causal association of cervical

cancer with this sexually transmitted viral infection, substantial interest has arisen to develop effective prophylactic and therapeutic vaccines. Prophylactic strategies currently under investigation focus on the induction of effective humoral and cellular immune responses that are potentially protective against subsequent HPV infection. Papillomavirus-like particles have been synthesized to induce neutralizing antibody responses, and impressive immunoprophylactic effects have been demonstrated in both animals and humans. For the treatment of existing HPV infection, techniques to augment cellular immunity by enhancing viral antigen recognition are under investigation. Vaccines targeting the oncogenic proteins E6 and E7 of HPV-16 and -18 are the focus of current clinical trials for cervical cancer patients. It is hoped that the development of successful HPV-specific vaccines will diminish the costs of existing cervical cancer screening programs and reduce the morbidity and mortality associated with the treatment of cervical neoplasias

Follow-up evaluation of a phase II prostate cancer vaccine trial.

Tjoa BA, Simmons SJ, Elgamal A, et al.

*Prostate*. 1999 Jul 1; 40(2):125-9.

**BACKGROUND:** A phase II trial, involving infusions of autologous dendritic cells (DC) and two human histocompatibility antigen (HLA-A2)-specific prostate-specific membrane antigen (PSMA) peptides, was recently completed. Thirty percent of the participants, including subjects with hormone-refractory metastatic disease, and those with suspected local recurrence of prostate cancer, were identified as clinical responders. This report describes the follow-up evaluation of 19 responders in the two study groups. **METHODS:** After conclusion of the study, study participants were subjected to follow-up evaluations at 6-8-week intervals. Each responder was reevaluated for response status, and duration of response was determined. **RESULTS:** Subjects were observed for an average of 291 days (metastatic group, group A-2) and 557 days (local recurrence group, group B), which included the treatment and follow-up periods. The average duration of response was 149 days for group A-2, and 187 days for group B. A majority of responders (11/19; 58%) were still responsive at the end of the current follow-up. **CONCLUSIONS:** The responses observed may be significant and relatively durable. This study suggests that DC-based cancer vaccines in the future may provide an additional therapy for advanced prostate cancer

Cancer Vaccine May Help Patients with Melanoma Spread to the Lungs.

TJUH.

Philadelphia, PA: Thomas Jefferson University Hospital. 2001

Generation of human cytotoxic T cells specific for human carcinoembryonic antigen epitopes from patients immunized with recombinant vaccinia-CEA vaccine.

Tsang KY, Zaremba S, Nieroda CA, et al.

*J Natl Cancer Inst*. 1995 Jul 5; 87(13):982-90.

**BACKGROUND:** The human carcinoembryonic antigen (CEA), which is expressed in several cancer types, is a potential target for specific immunotherapy using recombinant vaccines. Previous studies have shown that when the CEA gene is placed into vaccinia virus, the recombinant vaccine (rV-CEA) can elicit T-cell responses in both rodents and non-human primates. **PURPOSE:** Our objective was to determine if rVCEA could elicit CEA-specific T-cell responses in humans with appropriate human leukocyte antigen (HLA) motifs. **METHODS:** Peripheral blood lymphocytes (PBLs) obtained from patients with metastatic carcinoma, both before and after vaccination with rV-CEA, were analyzed for T-cell response to specific 9- to 11-mer CEA peptides selected to conform to human HLA class I-A2 motifs. **RESULTS:** While little or no T-cell growth was seen from preimmunization PBLs of patients pulsed with CEA peptides and interleukin 2 (IL-2), T-cell lines were obtained from PBLs of patients after vaccination with one to three cycles of stimulation. Cytolytic T-cell lines from three HLA-A2 patients were established with a 9-amino acid peptide (CAP-1), and the CD8+/CD4+ double-positive T-cell line (V24T) was chosen for detailed analysis. When autologous Epstein-Barr virus (EBV)-transformed B cells were either incubated with CAP-1 peptide or transduced with the CEA gene using a retroviral vector, they were lysed by the V24T cell line, but allogeneic non-A2 EBV-transformed B cells were not. The SW403 human colon carcinoma cell line, which is CEA positive and HLA-A2 positive, was also lysed by the V24T cell line, while two non-HLA-A2 CEA-positive colon carcinoma cell lines were not. To further confirm the class I HLA-A2 restricted nature of the V24T cytotoxicity, the non-HLA-A2 SW837 CEA-expressing colon carcinoma cell line was infected with a recombinant vaccinia virus expressing the HLA class I-A2 gene, and it became susceptible to V24T lysis. Cells infected with vector alone were not lysed. **CONCLUSIONS:** This study demonstrates for the first time (a) the ability to generate a human cytolytic T-cell response to specific epitopes of CEA, (b) the class I HLA-A2 restricted nature of the T-cell mediated lysis, and (c) the ability of human tumor cells to endogenously process CEA to present a specific CEA peptide in the context of major histocompatibility complex for T-cell-mediated lysis. **IMPLICATIONS:** These findings have implications in the development of specific second-generation cancer immunotherapy protocols

News Release: Experimental Lymphoma Vaccine Tested at UCLA's Jonsson Cancer Center; Volunteers Sought for Phase III Study 2001.

UCLA.

2001

News Release: UI Testing Vaccine for Cervical Cancer.

UI.

1998

Dendritic Cell Vaccine Helps Fight Children's Cancer.

UniSci.

2001;2001b

Promising Lung Cancer Vaccine Trial Results Reported.

UniSci.

2001;2001a

Vaccine Increases Survival with Late-Stage Metastases.

UniSci.

2001

Vaccination with HPV16 peptides of patients with advanced cervical carcinoma: clinical evaluation of a phase I-II trial.

van Driel WJ, Rensing ME, Kenter GG, et al.

*Eur J Cancer.* 1999 Jun; 35(6):946-52.

A phase I-II clinical trial was performed involving vaccination with HPV16 E7 peptides of patients suffering from HPV16 positive cervical carcinoma which was refractory to conventional treatment. Patients receiving the vaccine were HLA-A\*0201 positive with HPV16 positive cervical carcinoma. The clinical trial was designed as a dose-escalation study, in which successive groups of patients received 100 micrograms, 300 micrograms or 1000 micrograms of each peptide, respectively. The vaccine consisted of two HPV16 E7 peptides and one helper peptide emulsified in Montanide ISA 51 adjuvant. 19 patients were included in the study, no adverse side-effects were observed. 2 patients showed stable disease for 1 year after vaccination; 15 patients showed progressive disease of whom 1 died during the vaccination treatment due to progressive disease; and 2 patients showed tumour-regression after chemotherapy following vaccination. A relative low count of lymphocytes before and after vaccination was present in 11/19 patients indicating that these patients were immunocompromised. This study shows that HPV16 E7 peptide vaccination is feasible, even in a group of patients with terminal disease. This paves the way for vaccinating patients with less advanced disease, whose immune system is less compromised by progressive disease

Active specific immunotherapy for stage II and stage III human colon cancer: a randomised trial.

Vermorken JB, Claessen AM, van Tinteren H, et al.

*Lancet.* 1999 Jan 30; 353(9150):345-50.

BACKGROUND: Colon cancer is curable by surgery, but cure rate depends on the extent of disease. We investigated whether adjuvant active specific immunotherapy (ASI) with an autologous tumour cell-BCG vaccine with surgical resection was more beneficial than resection alone in stage II and III colon cancer. METHODS: In a prospective randomised trial, 254 patients with colon cancer were randomly assigned postoperative ASI or no adjuvant treatment. ASI was three weekly vaccinations starting 4

weeks after surgery, with a booster vaccination at 6 months with 10(7) irradiated autologous tumour cells. The first vaccinations contained 10(7) BCG organisms. We followed up patients for time to recurrence, and recurrence-free and overall survival. Analysis was by intention to treat. FINDINGS: The 5.3 year median follow-up (range 8 months to 8 years 11 months) showed 44% (95% CI 7-66) risk reduction for recurrence in the recurrence-free period in all patients receiving ASI (p=0.023). Overall, there were 40 recurrences in the control group and 25 in the ASI group. Analysis by stage showed no significant benefit of ASI in stage III disease. The major impact of ASI was seen in patients with stage II disease, with a significantly longer recurrence-free period (p=0.011) and 61% (18-81) risk reduction for recurrences. Recurrence-free survival was significantly longer with ASI (42% risk reduction for recurrence or death [0-68], p=0.032) and there was a trend towards improved overall survival. INTERPRETATION: ASI gave significant clinical benefit in surgically resected patients with stage II colon cancer. ASI has minimal adverse reactions and should be considered in the management of stage II colon cancer

Human papillomavirus is a necessary cause of invasive cervical cancer worldwide.

Walboomers JM, Jacobs MV, Manos MM, et al.

*J Pathol.* 1999 Sep; 189(1):12-9.

A recent report that 93 per cent of invasive cervical cancers worldwide contain human papillomavirus (HPV) may be an underestimate, due to sample inadequacy or integration events affecting the HPV L1 gene, which is the target of the polymerase chain reaction (PCR)-based test which was used. The formerly HPV-negative cases from this study have therefore been reanalyzed for HPV serum antibodies and HPV DNA. Serology for HPV 16 VLPs, E6, and E7 antibodies was performed on 49 of the 66 cases which were HPV-negative and a sample of 48 of the 866 cases which were HPV-positive in the original study. Moreover, 55 of the 66 formerly HPV-negative biopsies were also reanalyzed by a sandwich procedure in which the outer sections in a series of sections are used for histological review, while the inner sections are assayed by three different HPV PCR assays targeting different open reading frames (ORFs). No significant difference was found in serology for HPV 16 proteins between the cases that were originally HPV PCR-negative and -positive. Type-specific E7 PCR for 14 high-risk HPV types detected HPV DNA in 38 (69 per cent) of the 55 originally HPV-negative and amplifiable specimens. The HPV types detected were 16, 18, 31, 33, 39, 45, 52, and 58. Two (4 per cent) additional cases were only HPV DNA-positive by E1 and/or L1 consensus PCR. Histological analysis of the 55 specimens revealed that 21 were qualitatively inadequate. Only two of the 34 adequate samples were HPV-negative on all PCR tests, as against 13 of the 21 that were inadequate (  $p < 0.001$ ). Combining the data from this and the previous study and excluding inadequate specimens, the worldwide HPV prevalence in cervical carcinomas is 99.7 per cent. The presence of HPV in virtually all cervical cancers implies the highest worldwide attributable fraction so far reported for a specific cause of any major human cancer. The extreme rarity of HPV-negative cancers reinforces the rationale for HPV testing in addition to, or even instead of, cervical cytology in routine cervical screening

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